PATENT
Customer No. 22,852
Attorney Docket No. 04012.0373-00000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
R. W. Esmond et al.	)	Group Art Unit: 1614
	)	
Application No.: 09/394,712	)	Examiner: Vickie Y. Kim
	)	
Filed: September 13, 1999	)	
	)	
For: Method for Treating or Preventing Alzheimer's Disease	)	

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Commissioner for Patents
P.O. Box 1450
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Sir:

SUPPLEMENTAL REQUEST UNDER 37 C.F.R. § 1.607 FOR AN INTERFERENCE WITH U.S. PATENT NO. 6,191,154

Applicants hereby supplement their Request for Interference Under 37 C.F.R. § 1.607(a) filed March 29, 2001.

I. The Patent and Application

Applicants request that an interference be declared between the present application and U.S. Patent No. 6,191,154 entitled COMPOSITIONS AND METHODS FOR THE TREATMENT OF ALZHEIMER'S DISEASE, CENTRAL NERVOUS SYSTEM INJURY, AND INFLAMMATORY DISEASES issued February 20, 2001 (hereinafter the '154 patent) (attached as Exhibit 1). The '154 patent issued from Application No. 09/200,700 filed **November 27, 1998**.

The present application is a continuation of International Application No. PCT/US98/04731 filed March 12, 1998 (attached as Exhibit 2), which claims the benefit of U.S. Provisional Application No. 60/039,607 filed March 12, 1997 (attached as Exhibit 3). As further set forth in this request, the allowable claims in the present application are thus entitled to a priority date of **March 12, 1997**, more than 20 months before the filing date of the '154 patent.

II. An Interference is Appropriate

An interference is appropriate between an application and an unexpired patent owned by a different party when the application and the patent contain claims to the same patentable invention. 37 C.F.R. § 1.601(i). The test for ascertaining whether claims are directed to the same patentable invention is set forth in 37 C.F.R. § 1.601(n) as follows:

> Invention "A" is the *same patentable invention* as an invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A."

Under this test, Applicants' invention, as defined by claim 23 (invention "B") fully anticipates the '154 patent invention, as defined by claim 1 (invention "A"). Analogously, the '154 patent invention, as defined by claim 1 (invention "B"), fully anticipates Applicants' invention, as defined by claim 23 (invention "A"), assuming claim 1 of the '154 patent is prior art to application claim 23. The extensive overlap between these claims clearly shows that claim 1 of the '154 patent encompasses the same invention as defined by Applicants' pending claim 23 and vice versa. Accordingly, the two-way test for "same patentable invention" is satisfied in this case. *See, Eli Lilly & Co. v. Board of Regents of the University of Washington,* 334 F.3d 1264, 1268-70 (Fed. Cir. 2003), *cert denied,* 124 S.Ct. 1713 (2004).

A comparison of Applicants allowable claim 23 with claim 1 of the '154 patent makes is readily apparent that these claims are directed to the same invention, *i.e.,* they define interfering subject matter:

> **Applicants' Claim 23.** A method for the treatment of Alzheimer's disease, in a human, comprising administering to the human in need thereof an effective amount of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione.

> **'154 Patent Claim 1.** A method for treating Alzheimer's disease, comprising administering a therapeutically effective amount of at least one PPARγ agonist to a subject, wherein said PPARγ agonist is selected from the group consisting of troglitazone, ciglitazone, pioglitazone, BRL 49653, and englitazone.

The formula 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione and BRL 49653 are the same compound, commonly referred to as rosiglitazone. *See, Chemical Abstracts Registry,* Entry No. 122320-73-4 (American Chemical Society) attached as Exhibit 4. Thus, both claims are directed to the treatment of Alzheimer's disease by administration of rosiglitazone, the '154 patent including rosiglitazone as one of 5 possible compounds in a Markush group.

Applying the two-way test, Applicants' claim to a method for the treatment of Alzheimer's disease using rosiglitazone clearly anticipates the '154 patent claim to a method for treating Alzheimer's disease using a PPARγ agonist that includes rosiglitazone as a member of a Markush group. *See, Eli Lilly & Co. v. Barr Labs, Inc.*, 251 F.3d 955, 971 (Fed. Cir. 2001) (genus claim not patentable over earlier species claim); *In re Gosteli*, 872 F.2d 1008, 1010 (Fed. Cir. 1989) (genus of 21 specific chemical species in Markush claims anticipated by prior art reference disclosing two of the chemical species). Likewise, while a genus disclosure does not always anticipate a claim to a species within the genus, anticipation exists if the species is clearly named

within the disclosure, no matter how many other species are additionally named. M.P.E.P. § 2131.02 (8th ed., 2001) (citing *Ex Parte A*, 17 U.S.P.Q. 2d 1716 (Bd. Pat. App. & Inter. 1990)). Since claim 1 of the '154 patent specifically names BRL 49653 (rosiglitazone), the '154 patent would anticipate Applicants' claim 23 if it were prior art to such claim.

It should be noted that the mere identification of the subject compounds as a "PPARγ agonist" does not differentiate the claims of the '154 patent. It was known in the art that thiazolidinediones are PPARγ agonists. *J. Biol. Chem.*, Vol. 270, No. 22, 12953-56 (1995)(attached as Exhibit 5). Further, any PPARγ activity of the recited compounds would be an inherent property of such compounds.

III. Proposed Count

Applicants provide a proposed count (corresponding to Applicants' claim 23) pursuant to 37 C.F.R. § 1.601(f):

> A method for the treatment of Alzheimer's disease, in a human, comprising administering to the human in need thereof an effective amount of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione.

IV. Claims Corresponding to the Proposed Count

A claim should be designated as corresponding to the count if, considering the count as prior art, the claim would be unpatentable over the count under 35 U.S.C. § § 102 or 103. M.P.E.P. § 2309.02 (8th ed., 2001). In this case, assuming that the proposed count were prior art, claims 23-24, 28-29, 31 and 33 of the present application and claims 1-10 of the '154 patent would be unpatentable over the proposed count. As set forth below, those claims would be anticipated or rendered obvious by the proposed count.

A. Claims 1-10 of the '154 Patent Correspond to the Proposed Count

1. Claims 1-5

As set forth above, claim 1 of the '154 patent would be anticipated by the proposed count, which is identical to claim 23 of the present application. Claims 2-5 of the '154 patent depend on claim 1 and read as follows:

> 2. The method of claim 1, wherein said subject is selected from the group consisting of subjects identified as being susceptible to Alzheimer's disease and subjects suffering from Alzheimer's disease.
>
> 3. The method of claim 1, wherein said therapeutically effective amount of said PPARγ agonist is between 0.1 mg to 100 mg.
>
> 4. The method of claim 1, wherein said therapeutically effective amount of said PPARγ agonist comprises approximately 10 mg/kg per day.
>
> 5. The method of claim 1, wherein said administering comprises oral administering.

Simply put, none of these dependent claims are distinguishable over the proposed count. Claim 2 merely identifies the target patients as those "susceptible to" or "suffering from" Alzheimer's - the obvious patient groups one would treat. Claim 2 is not patentably distinct from claim 1 and should be designated as corresponding to the proposed count.

Dependent claims 3-5 merely add dosing limitations. U.S. Patent No. 5,478,852 (the '852 patent - attached as Exhibit 6) discloses rosiglitazone (col. 15, lines 28-29), that the quantity of active component in a unit dose preparation may be 0.1 mg to 100 mg (col. 17, lines 50-51), that a "daily dose range of about 0.01 mg to about 10 mg per kilogram is preferred" (col. 17, lines 62-63), and oral administration (col. 17, lines 10-12). Claims 3-5 are thus not patentably distinct from claim 1 and should be designated as corresponding to the proposed count.

2. Claims 6-10

Claim 6 of the '154 patent is virtually identical to claim 1, except that it is directed to the treatment of "a central nervous system injury." Claim 6 reads as follows:

> 6. A method for treating a central nervous system injury, comprising administering a therapeutically effective amount of at least one PPARγ agonist to a subject suffering from a central nervous system injury, wherein said PPARγ agonist is selected from the group consisting of troglitazone, ciglitazone, pioglitazone, BRL 49653, and englitazone.

Alzheimer's disease is generally understood to impair the brain and, specifically, nerve cells within the brain. *See, e.g.*, www.alzheimers.org (pertinent excerpts attached as Exhibit 7). In fact, the Wilkerson patent (cited in both the '154 patent and the present application) characterized Alzheimer's disease as a nervous system disorder. U.S. Patent No. 5,326,770 (col. 4, lines 32-35) (attached as Exhibit 8). Accordingly, claim 6 is not patentably distinct from claim 1 and should be designated as corresponding to the proposed count.

Dependent claims 7-9 add to claim 6 the same dosing limitations as in claims 3-5:

> 7. The method of claim 6, wherein said therapeutically effective amount of said PPARγ agonist is between 0.1 mg to 100 mg.
>
> 8. The method of claim 6, wherein said therapeutically effective amount of said PPARγ agonist comprises approximately 10 mg/kg per day.
>
> 9. The method of claim 6, wherein said administering step comprises oral administering.

As discussed above, the '852 patent discloses rosiglitazone (col. 15, lines 28-29), that the quantity of active component in a unit dose preparation may be 0.1 mg to 100 mg (col. 17, lines 50-51), that a "daily dose range of about 0.01 mg to about 10 mg per kilogram is preferred" (col. 17, lines 62-63), and oral administration (col. 17, lines 10-12). Claims 7-9 are thus not patentably distinct from claim 1 and should be designated as corresponding to the proposed count.

Dependent claim 10 recites types of central nervous system injury:

> 10. The method of claim 6, wherein said central nervous system injury comprises an injury selected from the group consisting of stroke, ischemic damage to said nervous system, and neural trauma.

While the causes of Alzheimer's disease continue to be investigated, it appears that damage to blood vessels in the brain, such as from stroke, may worsen the symptoms of Alzheimer's disease. *See, e.g.* www.alzheimers.org. (pertinent excerpts attached as Exhibit 7). Since claim 10 recites both "stroke" and "ischemic damage to said nervous system" and the treatment of patients "suffering from" Alzheimer's disease corresponds to the proposed count (*see, e.g.*, dependent claim 2), claim 10 is not believed to be patentably distinct from claim 1 and should be designated as corresponding to the count.

B. Application Claims 23-24, 28-29, 31 and 33 Correspond to the Proposed Count

Claim 23 is identical to the proposed count. Claims 24 and 31 are as follows:

> 24. A method for the treatment of Alzheimer's disease, in a human, comprising administering to the human in need thereof an effective amount of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione maleate.

> 31. A method for the treatment of Alzheimer's disease, in a human, comprising administering to the human in need thereof an effective amount of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione or a pharmaceutically acceptable salt thereof.

Claim 24 is identical to the proposed count except for reciting the use of the maleate salt of rosiglitazone. Claim 31 is identical to the proposed count except for reciting the use of rosiglitazone or "a pharmaceutically acceptable salt thereof." The maleate salt and other

pharmaceutically acceptable salts of rosiglitazone are disclosed in the '852 patent (col. 15, line 38 - col. 16, line 28), which is incorporated by reference in the present application. The methods of claims 24 and 31 are thus unpatentable over method claim 23 and, accordingly, claims 23, 24 and 31 should be designated as corresponding to the proposed count.

Claims 28-29 and 33 are similar to claims 23-24 and 31 except that they are directed to improving mentation of a patient with Alzheimer's diseases. These claims read as follows:

> 28. A method of improving mentation of a patient with Alzheimer's disease, comprising administering to said patient an effective amount of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione.

> 29. A method of improving mentation of a patient with Alzheimer's disease, comprising administering to said patient an effective amount of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione maleate.

> 33. A method of improving mentation of a patient with Alzheimer's disease, comprising administering to said patient an effective amount of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione or a pharmaceutically acceptable salt thereof.

The improvement of mentation or thought process of a patient with Alzheimer's is a form of treatment (*i.e.,* treating a symptom) of Alzheimer's disease. Also, as previously stated, the maleate salt and other pharmaceutically acceptable salts of rosiglitazone are disclosed in the '852 patent (col. 15, line 38 - col. 16, line 28). Thus, the methods of claims 28-29 and 33 are unpatentable over method claim 23 and claims 28-29 and 33 should be designated as corresponding to the proposed count.

V. Applicants' Specification Supports Claims 23-24, 28-29, 31 and 33

As noted above, the present application is a continuation of International Application No. PCT/US98/04731 filed March 12, 1998, which claims the benefit of U.S. Provisional Application No. 60/039,607 filed March 12, 1997. Support for Applicants' claims corresponding to the count are found in both of these prior applications, as well as the present application.

A. U.S. Provisional Application No. 60/039,607 filed March 12, 1997

Support for claims 23-24, 28-29, 31 and 33 appears in the provisional specification, including via the incorporation by reference of the '852 patent at page 10, lines 7-8. Treatment of, and improving mentation in, an Alzheimer's patient are disclosed at page 4, lines 2-23. The agents and administration thereof, as disclosed in the '852 patent, are disclosed at page 6, lines 18-28 of the provisional application. Support in the '852 patent for 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione (rosiglitazone) is at col. 15, lines 28-29. Support for the pharmaceutically acceptable salts (including maleate) is found at col. 15, line 38 - col. 16, line 28 of the '852 patent. Thus, Applicants' provisional application fully supports the claims corresponding to the proposed count.

B. International Application PCT/US98/04731 filed March 12, 1998

Support for claims 23-24, 28-29, 31 and 33 appears in the PCT specification, including via the incorporation by reference of the '852 patent at page 11, lines 21-23. Treatment of, and improving mentation in, an Alzheimer's patient are disclosed at page 4, line 12 - page 5, line 7. The agents and administration thereof, as disclosed in the '852 patent, are disclosed at page 7, lines 7-17 of the PCT application. Support in the '852 patent for 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione (rosiglitazone) is at col. 15, lines 28-29. Support for the pharmaceutically acceptable salts (including maleate) is found at col. 15, line 38 -

col. 16, line 28 of the '852 patent. Thus, Applicants' PCT specification fully supports the claims corresponding to the proposed count.

C. Present Application - Serial No. 09/394,712 filed September 12, 1999

Support for claims 23-24, 28-29, 31 and 33 appears in the specification, including via the incorporation by reference of the '852 patent at page 11, lines 24-25. Treatment of, and improving mentation in, an Alzheimer's patient are disclosed at page 4, line 18 - page 5, line 11. The agents and administration thereof, as disclosed in the '852 patent, are disclosed at page 7, lines 8-19 of the present application. Support in the '852 patent for 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione (rosiglitazone) is at col. 15, lines 28-29. Support for the pharmaceutically acceptable salts (including maleate) is found at col. 15, line 38 - col. 16, line 28 of the '852 patent. Thus, Applicants' specification fully supports the claims corresponding to the proposed count.

VI. The Application Claims Corresponding to the Proposed Count are Patentable

The Examiner's Office Action of April 7, 2004, indicated that claims 23-24, 28-29, 31 and 33 would be allowable if rewritten in independent form. Accordingly, Applicants have rewritten claims 23-24, 28-29, 31 and 33 in independent form, including all of the limitations of the base claim and any intervening claims. The application claims corresponding to the proposed count are thus patentable, as acknowledged by the Examiner.

VII. Relevant Dates

As demonstrated above, the present application is entitled to the benefit of the filing date of U.S. Provisional Application No. 60/039,607 filed March 12, 1997. Thus, the effective filing date of the present application is **March 12, 1997**. *See, e.g., Hyatt v. Boone,* 146 F.3d 1348, 1352 (Fed. Cir. 1998).

According to the face of the patent, the '154 patent issued from U.S. Application No. 09/200,700 filed November 27, 1998. Accordingly, the earliest effective filing date to which the '154 patent may be entitled is **November 27, 1998.**

Based on the foregoing, Applicants should be designated as the senior party in an interference on the proposed count.

VIII. The Requirements of 35 U.S.C. § 135(b) are Satisfied

In compliance with 35 U.S.C. § 135(b), Applicants claimed the same or substantially the same subject matter as the '154 patent prior to the expiration of the one-year period from issuance of the '154 patent. In fact, Applicants' compliance with 35 U.S.C. § 135(b) as to claims 23-24, 28-29, 31 and 33 was acknowledged by the Examiner in the Office Action of April 7, 2004.

IX. Conclusion

In view of the foregoing, Applicants submit that pending claims 23-24, 28-29, 31 and 33 are directed to allowable subject matter that is patentably indistinct from the subject matter of claims 1-10 of the '154 patent. Applicants have demonstrated their right to an effective filing date of March 12, 1997, which is earlier than the patentee's earliest possible effective filing date of November 27, 1998. Accordingly, Applicants respectfully request that the Patent Office declare an interference between the present application and the '154 patent.

In declaring the interference, the Patent Office is requested to define the count as proposed in this Request, designating all pending claims of this application and claims 1-10 of the '154 patent to correspond to the Count. Applicants further request that they be accorded benefit of the effective filing date of March 12, 1997, and be designated as senior party in the interference.

Finally, upon a determination by the Patent Office that an interference should be declared, Applicants respectfully request that the Patent Office issue a Notice suspending prosecution of this application pending declaration of an interference.

If any fees are due in connection with the filing of this Request for Interference, please charge such fees (or credit overpayment) to Deposit Account No. 06-0916.

Respectfully submitted,

Dated: June 9, 2004

FINNEGAN, HENDERSON, FARABOW,
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Linda Phillips